Remarks

I. Status of the Claims and the Specification

Upon entry of the foregoing amendments claims 1-15, 19, 21-34, 55 and 61-90 are pending in the application, with claims 1 and 63 being the independent claims. Claims 16-18, 20, 35-54 and 56-60 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. Pending claims 5, 9, 10, 12 and 30 have been withdrawn from consideration by the Examiner as not being directed to an elected species.

Amendment is sought to claims 1-15, 19, 22-25, 27-32, 34, 55, 61 and 62, and new claims 63-90 are sought to be entered. These amendments and new claims are supported, *inter alia*, by the originally filed claims and specification and, accordingly, do not introduce new matter. The entry and consideration of these new claims and claim amendments is respectfully requested.

II. Summary of the Office Action

In the Office Action of January 12, 2006 (hereinafter "the Office Action"), at pages 2 to 6, the Examiner has made of record the restriction requirement and, at page 2, Applicants' election of a restriction group and species.

At pages 6-7 of the Office Action the Examiner has rejected claims 1-3, 19, 20, 22-29 and 31 under 35 U.S.C. § 101 for allegedly reading on a product of nature.

At pages 7-8 of the Office Action the Examiner has rejected claims 1-4, 6-8, 11, 13-29, 31-40, 42-48, 51-53, 55, 61 and 62 under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. At pages 8-9 of the Office Action the Examiner

has rejected claims 1-4, 6-8, 11, 13-29, 31-40, 42-48, 51-53, 55, 61 and 62 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement.

At page 9 of the Office Action the Examiner has rejected claims 1-3, 19, 20, 22-29 and 31 under 35 U.S.C. § 102(b) as allegedly being anticipated by Woody *et al.* (Woody, M.A., *et al.* "Replication of coliphage Q beta as affected by host cell number, nutrition, competition from insusceptible cells and non-FRNA coliphages" J. Appl. Microb. (April 1997) 82, (4): 431-440), hereinafter "Woody *et al.*").

At pages 9-11 of the Office Action the Examiner has rejected claims 4, 6-8, 11, 13, 14, 21, 32-40, 42, 43, 48, 51-53, 55, 61 and 62 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Nakazato *et al.* (Nakazato, M., *et al.* "A role for ghrelin in the central regulation of feeding" *Nature* (January 2001) 409: 194-198, hereinafter "Nakazato *et al.*") in view of Vasiljeva *et al.* (Vasiljeva, I., *et al.* "Mosaic Q beta coats as a new presentation model" *FEBS* (1998) 431: 7-11, hereinafter "Vasiljeva *et al.* "). Furthermore, at pages 11-12 the Examiner has rejected claims 15-18 and 44-47 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Nakazato *et al.* in view of Vasiljeva *et al.*, as discussed above, and further in view of Lechner *et al.* (Lechner, F., *et al.*, "Virus-Like Particles as a Modular System for Novel Vaccines" *Intervirology* (2002) 45: 212-217, hereinafter "Lechner *et al.*").

In view of the following remarks, Applicants traverse the Examiner's rejections and respectfully request that they be reconsidered and withdrawn.

III. Election/Restriction and Examiner's telephone interview with Applicants

In the Office Action at page 2, the Examiner has made of record the telephonic interview between the Examiner and Applicants' representative on November 28, 2005, in

which Applicants' representative elected to prosecute the invention of Group I, encompassing claims 1-55, 61 and 62. For purposes of search and examination, Applicants' representative elected the species (xiii), Qβ bacteriophage, which is recited in claims 4, 7, 8, 14, 43 and 48; and the ghrelin peptide having the sequence of SEQ ID NO: 31, which is recited in claims 25, 52 and 53.

The Office Action at pages 4 and 5 now also states a requirement for election of species from claims 12 and 30. However, Applicants note that the Examiner did not require the election of species in claims 12 or 30 in the November 28, 2005, telephone interview.

MPEP § 808.1 states:

> In applications where only generic claims are presented, restriction cannot be required unless the generic claims recite such a multiplicity of species that an unduly extensive and burdensome search would be necessary to search the entire scope of the claim. See MPEP § 803.02. If applicant presents species claims to more than one patentably distinct species of the invention after an Office action on only generic claims, with no restriction requirement, the Office may require the applicant to elect a single species for examination.

That the Examiner was able to conduct the search and examination of the generic or linking claims without an election of species in claims 12 and 30 indicates that an election of species from claims 12 and 30 clearly was not required to prevent an undue search burden on the Examiner. Accordingly, it is believed that this requirement for an election of species is improper and should be reconsidered and withdrawn. If, however, an election of species is deemed to be proper, then Applicants hereby elect the species (a), SEQ ID NO:4, from claim 12; and species (b), SEQ ID NO:65, from claim 30. These elections are made without traverse.

Pursuant to the election of species, the Examiner has withdrawn from consideration claims 5, 9, 10, 12, 30, 41, 49, 50 and 54 as being drawn to nonelected species. The

Examiner has also withdrawn claims 56-60 as being drawn to a nonelected invention. Applicants have cancelled claims 16-18, 35-54 and 56-60 without prejudice or disclaimer solely to advance prosecution. Applicants reserve the right to prosecute claims to the cancelled subject matter in one or more continuing applications.

IV. Rejections under 35 U.S.C. § 101

In the Office Action at pages 6-7, the Examiner has rejected claims 1-3, 19, 20, 22-29 and 31 under 35 U.S.C. § 101 for allegedly reading on a product of nature. As an initial matter, claim 20 has been cancelled. Applicants respectfully traverse this rejection as it may have been applied to the presently pending claims.

At page 7 of the Office Action, the Examiner asserts that:

> These claims are drawn to a composition comprising a core particle having a first attachment site, and a ghrelin polyprotein having a naturally occurring second attachment. Ghrelin is naturally produced in the body. Thus, a human infected with a virus (i.e. a core particle) would comprise the claimed composition.

Applicants respectfully disagree, as the Examiner's rejection appears to be based, at least in part, on a misreading of claim 1. Claim 1 recites, in part:

> wherein said second attachment site associates with said first attachment site; and wherein said ghrelin or ghrelin peptide and said core particle interact through said association to form an ordered and repetitive antigen array.

Thus, claim 1 *requires* that the ghrelin or ghrelin peptide associates with the core particle to form an ordered and repetitive antigen array. The specification provides numerous examples of ways in which ghrelin/ghrelin peptide can associate, such as by fusion, nonpeptide covalent bonds, hydrophobic interactions, ionic or polar interactions, through hetero- or homo-bifunctional cross linkers and the like. *See, e.g.,* paragraphs [0046] and [0171] in the specification.

The fact that a human infected with a virus would simultaneously comprise both a ghrelin and a core particle is irrelevant, because neither the ghrelin and the virus would be *associated to form an ordered and repetitive array*, as required by the claim. Such a *combination* of elements is not found in nature, nor has the Examiner shown that ghrelin or ghrelin peptide naturally associates with a core particle to form an ordered and repetitive array.

Naturally occurring elements combined in a form that is not naturally occurring has been held to be patentable subject matter under 35 U.S.C. § 101. *See Diamond v. Chakrabarty*, 447 U.S. 303 (1980). There, the Supreme Court distinguished Chakrabarty's invention from a "handiwork of nature," stating that:

> [Chakrabarty's] claim is not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter - a product of human ingenuity "having a distinctive name, character [and] use." *Hartranft v. Wiegmann*, 121 U.S. 609, 615 (1887).

447 U.S. at 309-310. Just as the *Chakrabarty* Court, *id.*, had found that a non-natural combination of naturally occurring elements is patentable subject matter, Applicants' claimed composition comprises elements that may occur naturally, but which are combined in a form that is not naturally occurring-- they are associated to form an ordered and repetitive array. Such a "nonnaturally occurring manufacture or composition of matter" is within the scope of patentable subject matter under 35 U.S.C. § 101. *Id.* Applicants respectfully request reconsideration and withdrawal of the rejection.

V. Rejections under 35 U.S.C. § 112, second paragraph

In the Office Action at pages 7-8 the Examiner has rejected claims 1-4, 6-8, 11, 13-29, 31-40, 42-48, 51-53, 55, 61 and 62 under 35 U.S.C. § 112, second paragraph, as being

indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As an initial matter, claims 16-18, 20, 35-54, 56-60 have been cancelled, rendering moot any rejections of those claims. Applicants respectfully traverse the rejection as it may have been applied to the presently pending claims.

According to the U.S. Court of Appeals for the Federal Circuit:

> As mandated by the definiteness requirement of 35 U.S.C. §112, second paragraph, a specification shall include claims "*particularly pointing out and distinctly claiming* the subject matter which the applicant regards as his invention" (*emphasis* added). Determining whether a claim is definite requires an analysis of "whether one skilled in the art would understand the bounds of the claim when read in light of the specification . . . . If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, §112 demands no more." *Miles Lab., Inc. v. Shandon, Inc.*, 997 F.2d 870, 875 (Fed. Cir. 1993).

Personalized Media Communications v. ITC, 161 F.3d 696, 705 (Fed. Cir. 1998) (emphasis in original). Applicants assert that the present claims meet the definiteness requirement of 35 U.S.C. § 112, second paragraph, as construed by the courts, including in *Personalized Media, id.*, and will address each of the Examiner's rejections in turn.

At page 7, The Examiner has rejected claim 1 as indefinite in the recitation of "naturally occurring," because:

> one skilled in the art would not be able to determine whether the claimed attachment site is naturally occurring. This results because ghrelin mutations could exist in nature that would not be known to the skilled artisan.

Applicants respectfully disagree.

The Examiner appears to assert that the claim is indefinite because the skilled artisan does not know all possible naturally occurring ghrelin sequences, including mutants. However, this level of detail is not required for a claim to meet the requirements of 35 U.S.C. § 112, second paragraph. That a ghrelin mutant could exist in nature that would not be

known to the skilled artisan does not render claim 1 indefinite. *All* that is required is that "one skilled in the art would understand the bounds of the claim when read in light of the specification . . . . If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention." *Personalized Media,* 161 F.3d at 705.

Not only is the term "naturally occurring" clear to those of ordinary skill in the art, but the term "natural origin" and, by comparison, "non-natural" and "non-natural origin" are defined in the specification at paragraphs [0064] to [0066]. In the context of the second attachment site, those of "non-natural origin" are further exemplified in paragraph [0048], which recites "a second attachment site, which is of non-natural origin, i.e. not naturally occurring within the antigen or antigenic determinant, these antigen or antigenic constructs comprise an 'amino acid linker.'" The specification also provides examples of both naturally occurring and non-natural attachment sites. *See, e.g.,* paragraphs [0171]-[0178] of the specification.

In view of the specification, it would be clear to a person of ordinary skill that if a second attachment site were to be introduced into ghrelin by, for example, genetic engineering, then such an attachment site would be non-natural. On the other hand if, in a genetic fusion construct, ghrelin is attached via N- and C-termini, which naturally occur in ghrelin, then this would be an attachment site naturally occurring with said antigen or antigenic determinant.

For these reasons, Applicants respectfully assert that one of ordinary skill in the art would understand the term "naturally occurring" as used in the claims, both by its clear meaning and also when read in light of the specification. Indeed, in making the rejection under 35 U.S.C. § 101, the Examiner states that the claims are "drawn to a composition

comprising . . . a ghrelin polyprotein having a naturally occurring second attachment. Ghrelin is naturally produced in the human body." It would therefore appear that the Examiner is also reasonably apprised of the meaning of "naturally occurring" as it is used in claim 1. It would be incongruous for the Examiner to both correctly construe and use this term in rejecting claims and then, in the same Office Action, reject many of the same claims on the ground that this term is indefinite. Rather, the Examiner's proper use of the same term would appear to indicate that the term is definite since, "[i]f the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention" the claim is definite. *Personalized Media,* 161 F.3d at 705

Accordingly, Applicants have reasonably apprised those of ordinary skill in the art of the scope of the presently claimed invention, and therefore have fulfilled the requirements of 35 U.S.C. § 112, second paragraph. Claim 1 and claims 2-15, 19, 21-34, 55, 61 and 62 , which all depend from and incorporate the elements of claim 1, are therefore not indefinite under 35 U.S.C. § 112.

In the Office Action at page 7 the Examiner has rejected claim 13 as indefinite because:

> it is unclear how the phage genome is affected by Applicants' use of "mutant." A mutant coat protein may be a naturally occurring variant, or a recombinantly produced protein. In other words, the use of "mutant" fails to particularly point out and distinctly claim the composition of the coat protein.

Applicants respectfully disagree. As an initial matter, how the phage genome is affected by Applicants' use of the word "mutant" is irrelevant to patentability under 35 U.S.C. § 112, second paragraph. The only thing relevant is whether a person of ordinary skill in the art is reasonably apprised of the scope of the term "mutant" as it operates in the claims. Further,

whether a mutant variant was originally obtained by isolation, selection or specifically constructed *in vitro* does not, by itself, make the term indefinite as it operates in the claim.

The term "mutant" is well known and understood by those of ordinary skill in the art. Moreover, the specification provides examples of the making and using recombinant mutant proteins. For example, paragraphs [0123]-[0197] and Example 1 describe the generation of mutant variants of bacteriophage coat proteins and Hepatitis B core. As a person of ordinary skill would be reasonably apprised of the scope of the invention of claim 13, both from the plain language of claim 13 and by reference to the specification, Applicants assert that claim 13 is not indefinite.

At page 8 of the Office Action, the Examiner has rejected claims 28 and 29 as indefinite for lacking antecedent basis for "said amino acid linker" in claim 1. Applicants have removed from claims 28 and 29 the dependency on claim 1, rendering moot the Examiner's rejection.

For at least the above reasons, claims 1-15, 19, 21-34, 55, 61 and 62 are not indefinite under 35 U.S.C. § 112, second paragraph. The Examiner is respectfully requested to reconsider and withdraw the rejection. Applicants also assert that new claims 63-90 are also not indefinite, for at least the reasons outlined above and as applied to new claims 63-90.

VI. Rejections under 35 U.S.C. § 112, first paragraph, written description

In the Office Action at pages 8-9, the Examiner has rejected claims 1-4, 6-8, 11, 13-29, 31-40, 42-48, 51-53, 55, 61 and 62 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. At page 8 of the Office Action, the Examiner asserts:

> Applicants claim any second attachment site on an antigenic ghrelin peptide that is naturally occurring, or non-naturally occurring. However, the specification fails to provide written description support for the breadth of the claimed second attachment site. Moreover, the molecular interactions between an unspecified "core particle" and a ghrelin peptide would be complex such that the skilled artisan would not be able to determine those core particles that would interact with the claimed attachment site.

Applicants respectfully disagree. As an initial matter, claims 16-18, 20, 35-54 and 56-60 have been cancelled, rendering moot the rejection as it was applied to those claims. Applicants respectfully traverse the rejection as it may have been applied to the presently pending claims.

(a) Construction of the claims

In view of the Examiner's rejection under 35 U.S.C. § 101, Applicants respectfully believe that the Examiner has misconstrued the claims, and thus is attempting to apply the law to an invention that is of a scope different from that which is presently claimed. Applicants therefore reiterate herein the comments made above in the context of the rejection under 35 U.S.C. § 101.

Furthermore, claim 1 recites that:

> said second attachment site associates with said first attachment site; and wherein said ghrelin or ghrelin peptide and said core particle interact through said association to form an ordered and repetitive antigen array.

It is clear from the language of claim 1 that the second and first attachment sites associate to form an ordered and repetitive array. That is, both first and second attachment sites are understood as inherently performing a function in the claimed composition. Accordingly, Applicants do not claim "any second attachment site on an antigenic ghrelin peptide that is naturally occurring, or non-naturally occurring," as the Examiner has asserted. Rather than

claiming the second attachment site *per se*, claim 1 is drawn to a composition in which the second attachment site is understood to be a way by which ghrelin or ghrelin peptide associates with the core particle to form an ordered and repetitive antigen array. Similarly, the first attachment site is understood to be a way by which the core particle associates with ghrelin or a ghrelin peptide to form an ordered and repetitive antigen array. Therefore, the claimed invention recites that the core, antigen, first attachment site and second attachment site are present in a particular relationship. Applicants assert that the scope of the invention as a whole is well within the written description provided by the specification. Furthermore, the scope of each element in claim (genera of core, antigen, first attachment site and second attachment) is consonant with the written description provided by the specification, as viewed by a person of ordinary skill in the art.

(b) The scope of the presently claimed invention is consonant with the written description provided by the specification.

Whether the Examiner's rejection applies to the entire claim or to any element therein, Applicants assert that the claim and its elements are fully supported by the specification.

The crux of the question concerning whether a claimed invention is adequately described is whether one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention in the specification as filed. *See Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1320 (Fed. Cir. 2003) (citing *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991)); *see also* M.P.E.P. § 2163.02. The Federal Circuit in *Eli Lilly* set forth several tests for whether a claimed genus is adequately described, including the "representative number of species" test and the "common structural features" test. *Regents of the Univ. of Calif. v. Eli Lilly & Co.*, 43 U.S.P.Q.2d 1398,

1406 (Fed. Cir. 1997). However, the court also stated that "[w]e will not speculate in what *other ways* a broad genus of genetic material may be properly described." *Id.* (emphasis added). It is also important to recognize that the specification does not have to describe that which is already in possession of those of ordinary skill in the art. *See, e.g., Capon v. Eshhar,* 481 F.3d 1349, 76 U.S.P.Q.2d 1078 (Fed. Cir. 2005); *See also Invitrogen Corp. v. Clontech Lab., Inc.,* 429 F.3d 1052, 1073 (Fed. Cir. 2005).

Thus, there is no fixed set of tests for whether a claimed genus is adequately described. Instead, the determination of compliance with the written description requirement is a fact-based one and, in cases subsequent to *Eli Lilly*, the Federal Circuit has limited the holding in *Eli Lilly* to its particular set of facts. *See, e.g., Moba* at 1320; s*ee also Amgen Inc. v. Hoechst Marion Roussel Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003); *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 63 U.S.P.Q.2d 1609, 1613 (Fed. Cir. 2002).

Under this law, therefore, the present application not only meets but greatly exceeds the written description requirement under 35 U.S.C. § 112, first paragraph. The genus of core particles with first attachment sites is described in detail. For example, the following points in the specification provide explicit definitions for the terms: first attachment site, [0047]; core particle, [0051]; and specific examples of core particles such as a virus, a virus-like particle, a bacteriophage, a virus-like particle of a RNA-phage, a bacterial pilus or flagella or any other core particle having an inherent repetitive structure capable of forming an ordered and repetitive antigen array, [0015]. Paragraphs [0089] to [0186] describe and list over one hundred different types of core particles suitable for use in the present invention, including different DNA and RNA viruses, bacteriophage, pili, coat proteins, mutant variants, and the like, including specific sequences thereof; and also describe how to modify core particles to

affect the numbering and positions of the first attachment sites. Working examples of modifications of the core particle to introduce novel first attachment sites are provided in the specification at, for example, Example 1 and in prior related Applications which have been incorporated by reference into the specification, including PCT publications WO 00/32227, WO 01/85208, and WO 02/056905.

The genus of ghrelin and ghrelin peptides with second attachment sites is similarly defined, described and exemplified. For example, definitions are provided for second attachment site and ghrelin at paragraphs [0048] and [0058]. Paragraphs [0212] to [0237] describe more than 30 species of ghrelin and at least 34 species of ghrelin with second attachment sites added, linkers, and the like.

Not only are the individual genera described in great detail, but the specification describes the *relationship* between the core particle with first attachment site and the ghrelin/ghrelin peptide with second attachment site. This includes ways to link the elements, the number of antigens per core particle, their spacing and more. *See, e.g.* paragraphs [0067], [0083], and [0171]-[0186]. Applicants also describe a number of working embodiments (*See, e.g.*, Examples 16-18).

Having described more than a sufficient "representative number of species" and having *also* described "common structural features," Applicants have clearly exceeded the requirements of 35 U.S.C. § 112, first paragraph, as construed under *Eli Lilly,* 43 U.S.P.Q.2d 1398, and its progeny. As the scope of claim 1 is within the scope of the written description provided by the specification, Applicants respectfully believe that the scope of the pending claims which depend from it are within the scope of the specification. Accordingly, Applicants respectfully request the reconsideration and withdrawal of the rejection of claims

1-15, 19, 21-34, 55, 61 and 62 under 35 U.S.C. § 112, first paragraph, written description. Applicants also respectfully believe that new claims 63-90 are also fully supported by the written description provided by the specification.

VI. Rejections under 35 U.S.C. § 102

In the Office Action at page 9, the Examiner has rejected claims 1-3, 19, 20, 22-29 and 31 under 35 U.S.C. § 102(b) as allegedly being anticipated by Woody *et al.* Applicants respectfully disagree. As an initial matter, claim 20 is cancelled, rendering moot the rejection of that claim. Applicants therefore traverse the rejection as it may be applied to the presently pending claims.

The Woody *et al.* abstract cited by the Examiner describes the bacteriophage Qβ, which infects *E. coli,* which colonizes the human intestine. The fact that humans may simultaneously contain both ghrelin and bacteriophage Qβ does not, however, anticipate the *claimed* invention, which requires (in this particular embodiment) that ghrelin and bacteriophage Qβ associate through said second and first attachment sites to form an ordered and repetitive antigen array.

To anticipate a claimed invention, a single prior art reference must disclose each and every material element of the claim. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987). Because Woody *et al.* does not teach the association of ghrelin and bacteriophage Qβ through second and first attachment sites to form an ordered and repetitive antigen array, Woody *et al.* cannot anticipate the presently claimed invention.

Accordingly, claim 1 is not anticipated by Woody *et al.* Further, since claims 1-15, 19, 21-34, 61 and 62 depend from claim 1, they incorporate all elements of claim 1 (35 U.S.C. § 112) and are similarly not anticipated by Woody *et al.* Applicants also believe that new claims 63-90 are similarly free from this reference, for at least the reasons elaborated herein. Applicants therefore respectfully request that the Examiner reconsider and withdraw the present rejection under 35 U.S.C. § 102(b).

VII. Rejections under 35 U.S.C. § 103

(a) Claims 4, 6-8, 11, 13, 14, 21, 32-40, 42, 43, 48, 51-53, 55, 61 and 62 are not rendered obvious under 35 U.S.C. § 103 by Nakazato et al. in view of Vasiljeva et al.

In the Office Action at pages 10 to 11 the Examiner has rejected claims 4, 6-8, 11, 13, 14, 21, 32-40, 42, 43, 48, 51-53, 55, 61 and 62 under 35 U.S.C. § 103 as being rendered obvious by Nakazato *et al.* in view of Vasiljeva *et al.* Applicants respectfully disagree. As an initial matter claims 16-18, 35-54 and 56-60 have been cancelled, rendering moot the rejection as it may have been applied to those claims. Applicants traverse the rejection as it may have been applied to the presently pending claims.

The Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *See In re Piasecki*, 223 USPQ 785, 787-88 (Fed. Cir. 1984). The Examiner can satisfy this burden only by showing some objective teaching in the prior art, or that knowledge generally available to one of ordinary skill in the art, would lead that individual to combine the relevant teachings of the references in such a way as to produce the invention as claimed. *See In re Fine*, 5 USPQ2d 1596,1598 (Fed. Cir. 1988).

If a combination of references is used to attempt to establish obviousness, there must be "a reason, suggestion, or motivation in the prior art that would lead one of ordinary skill in

the art to combine the references, and that would also suggest a reasonable likelihood of success." *See Smiths Indus. Med. Sys. v. Vital Signs, Inc.*, 183 F.3d 1347, 1356 (Fed. Cir. 1999). "Such a suggestion or motivation may come from the references themselves, from knowledge by those skilled in the art that certain references are of special interest in a field, or even from the nature of the problem to be solved." *Id.* at 1347. Although the references "need not expressly teach that the disclosure contained therein should be combined, the showing of combinability must be 'clear and particular.'" *Ruiz v. A.B. Chance*, 234 F.3d 654, 665 (Fed. Cir. 2000). A rigorous application of the requirement for showing a suggestion or motivation to combine references aids in avoiding an impermissible hindsight reconstruction of the claimed invention. *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999).

In the Office Action at pages 10-11, the Examiner states that:

> Nakazato et al. disclose using an antigenic ghrelin peptide to vaccinate a rabbit for the production of polyclonal anti-ghrelin antibodies (see "Immunoneutralization" p197). Nakazato et al. do not expressly teach administering ghrelin in conjugation with Q beta phage to form an ordered and repetitive antigen array. However, Vasiljeva et al. disclose using Q beta phage capsid as a carrier for the administration of antigenic peptides. Vasiljeva et al. teach that using Q beta phage as an antigenic carrier is advantageous because Q beta phage particles (i) can-self assemble without viral RNA, (ii) is noninfectious, and (iii) can present between 25 and 86 copies of antigen per capsid shell. Thus, one skilled in the art would be motivated to present Nakazato et al.'s ghrelin antigen on a Q beta phage carrier to achieve these advantages. Moreover, such a combination would enjoy a reasonable expectation of success since a chimeric Q beta phage capsid assembly can easily be produced through recombinant DNA technology. It therefore would have been obvious to combine Nakazato et al. and Vasiljeva et al. to arrive at the claimed invention.

Applicants respectfully disagree with this statement for at least the following reasons.

First, Nakazato *et al.* does *not* describe using an antigenic ghrelin peptide to vaccinate rabbits for the production of ghrelin antibodies, as is asserted. The Examiner refers to the "Immunoneutralization" section on page 197 of Nakazato, which recites:

> We subjected anti-ghrelin antiserum to Affi-gel protein A affinity and then CNBr-Sepharose-coupled ghrelin affinity chromatography. We determined the amount of purified IgG by using a DC protein assay kit (Bio-Rad).

This section of Nakazato *et al.* does *not* disclose using an antigenic ghrelin peptide to vaccinate a rabbit for the production of polyclonal anti-ghrelin antibodies, nor is this disclosed elsewhere in Nakazato *et al.* All that is disclosed in Nakazato *et al.* is the use of anti-ghrelin antiserum. Nowhere does Nakazato *et al.* disclose how such antiserum was obtained, including the immunogen, conjugation conditions, immunization conditions, the level and type of antibodies obtained, *etc.*

To be available as a prior art reference, the publication must describe the claimed invention with sufficient enabling detail to place the public in possession of the invention. *See In re Donohue*, 766 F.2d 531, 533 (Fed. Cir. 1985); *see also PPG Industries, Inc. v. Guardian Industries Corp.*, 75 F.3d 1558, 1566 (Fed. Cir. 1996). The exceedingly sparse disclosure of Nakazato *et al.* does not provide sufficient disclosure for one of ordinary skill to practice immunization of an animal with ghrelin or ghrelin peptide to obtain antibodies. Nakazato *et al.* is therefore not an enabling disclosure and, therefore, does not provide the element that is asserted and cannot be used as a reference against the present claims.

Second, the very limited disclosure of Vasiljeva *et al.* does not remedy the defects of Nakazato *et al.* The Examiner has asserted that:

> Vasiljeva et al. teach that using Q beta phage as an antigenic carrier is advantageous because Q beta phage particles (i) can-self assemble without

> viral RNA, (ii) is noninfectious, and (iii) can present between 25 and 86 copies of antigen per capsid shell.

However, neither Vasiljeva *et al.* nor the Examiner explains the nexus between these properties and the presently claimed composition, which is not limited to these properties. Accordingly, both Vasiljeva *et al.* and Nakazato *et al.* fail to disclose or suggest the presently claimed invention, and the manifest defects of each reference are not remedied by combination with the other.

Third, even if there were sufficient disclosure, neither reference provides a motivation to combine it with the other and the Examiner has not otherwise provided explicit objective evidence that one of ordinary skill in the art would have been motivated to combine these references. "The showing of combinability must be 'clear and particular.'" *Ruiz v. A.B. Chance*, 234 F.3d 654, 665 (Fed. Cir. 2000). Moreover, the requisite motivation to combine references must be found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. *See In re Kotzab,* 217 F.3d 1365, 1370 (Fed. Cir. 2000); *see also In re Dow Chem. Co.,* 837 F.2d 469, 473 (Fed. Cir. 1988). In the present case, the cited art provides no motivation to combine and the Examiner has not pointed to any explicit knowledge allegedly available to one of ordinary skill that would supply this motivation. Accordingly, there is no basis on which to combine Nakazato *et al.* with Vasiljeva *et al.* Therefore, the Examiner has not met the burden of establishing a *prima facie* case of obviousness.

For at least these reasons, the presently claimed invention is not rendered obvious by Vasiljeva *et al.* or Nakazato *et al.,* alone or combination. Applicants therefore respectfully request that the Examiner reconsider and withdraw the present rejection of pending claims 4,

6-8, 11, 13, 14, 21, 32-34, 55, 61 and 62 under 35 U.S.C. § 103. For at least these reasons, Applicants also assert that new claims 63-90 are also nonobvious.

(b) Claims 15-18 and 44-47 are not rendered obvious under 35 U.S.C. § 103 by Nakazato et al. in view of Vasiljeva et al. and further in view of Lechner et al.

The Examiner has rejected claims 15-18 and 44-47 as obvious in view of the combination of Nakazato *et al.*, Vasiljeva *et al.* and Lechner *et al.* Applicants respectfully traverse. Nevertheless, as claims 16-18 and 44-47 have been cancelled, the rejection of those claims is rendered moot. Applicants respectfully traverse the rejection as it may have been applied to pending claim 15 and new claims 63-90.

For reasons elaborated above, which are entirely incorporated herein by reference, Nakazato *et al.* and Vasiljeva *et al.* would not have rendered the claims obvious under 35 U.S.C. § 103. The defects in these references cannot be remedied by combination with Lechner *et al.*, at least because the Examiner has not demonstrated a motivation to combine Lechner *et al.* with the other two references with reasonable expectations of success.

Nevertheless, these issues are moot as Lechner *et al.* is unavailable as prior art to the present claims. According to the Medline database, Lechner *et al.* was apparently published electronically on February 5, 2003, ahead of print publication on April 16, 2003. A printed copy of this publication information from the Medline database is attached as Exhibit A. The present Application was filed July 18, 2003, and claims benefit of the filing date of U.S. Provisional Patent Application No. 60/396,638, filed July 19, 2002. Hence, as Lechner *et al.* was published after the priority date to which the present claims are entitled, it is not available as prior art to the present claims.

For at least these reasons, Applicants assert that claims 15 and 63-90 are not rendered obvious under 35 U.S.C. § 103 by Nakazato *et al.* in view of Vasiljeva *et al.*, and further in view of Lechner *et al.* Applicants respectfully request that the Examiner reconsider and withdraw the present rejection.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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